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Biocomplexity Institute & Initiative

University of Virginia

Estimation of COVID-19 Impact in Virginia

December 22nd, 2020

(data current to December 19th – 21st)
Biocomplexity Institute Technical report: TR 2020-161



BIOCOMPLEXITY INSTITUTE

biocomplexity.virginia.edu

About Us

- Biocomplexity Institute at the University of Virginia
 - Using big data and simulations to understand massively interactive systems and solve societal problems
- Over 20 years of crafting and analyzing infectious disease models
 - Pandemic response for Influenza, Ebola, Zika, and others



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Overview

• Goal: Understand impact of COVID-19 mitigations in Virginia

Approach:

- Calibrate explanatory mechanistic model to observed cases
- Project infections for next 4 months
- Consider a range of possible mitigation effects in "what-if" scenarios

Outcomes:

- Ill, Confirmed, Hospitalized, ICU, Ventilated, Death
- Geographic spread over time, case counts, healthcare burdens

Key Takeaways

Projecting future cases precisely is impossible and unnecessary. Even without perfect projections, we can confidently draw conclusions:

- Case rate growth in Virginia slows and steadies with mixed patterns across commonwealth
- VA mean weekly incidence (43/100K) steady (from 44) as national surge slows and is slightly down for first week in months (to 59/100K from 66/100K).
- Recent updates:
 - Preliminary estimates for vaccination impact
 - Planning scenarios remain on Christmas holiday, starting Dec 24th
- Behavioral changes can outpace impact of optimistic vaccine rollout and prevent significantly more cases by Spring
- The situation is changing rapidly. Models will be updated regularly.



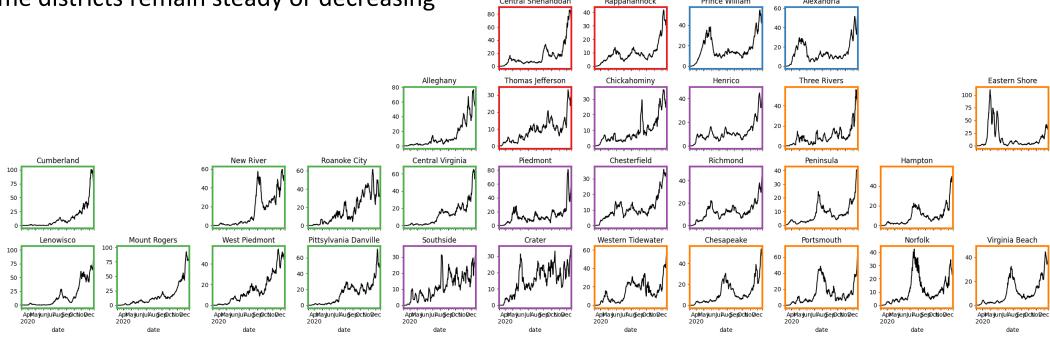
Situation Assessment



Case Rate (per 100k) by VDH District

Surging Rates continue

- Majority of districts have increasing rates
- Many districts experiencing highest rates of pandemic
- Some districts remain steady or decreasing



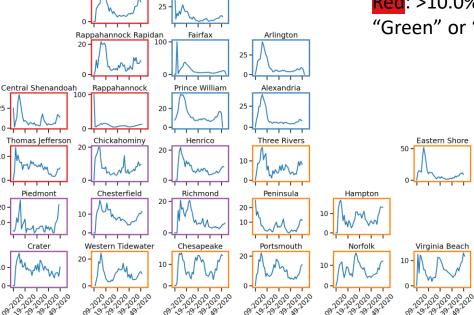


Test Positivity by VDH District

Weekly changes in test positivity by district

 Increasing levels in many districts throughout the commonwealth with many districts above 10% for several weeks

101 counties reporting over 10% on Dec 9



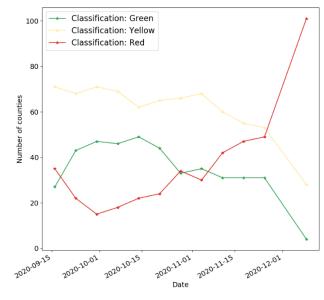
County level test positivity rates for RT-PCR tests.

Green: Test positivity < 5.0% (or with < 20 tests in past 14 days)

Yellow: Test positivity 5.0%-10.0% (or with <500 tests

and <2000 tests/100k and >10% positivity over 14 days)

Red: >10.0% and not meeting the criteria for "Green" or "Yellow"





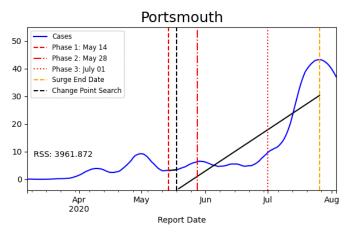


District Trajectories

Goal: Define epochs of a Health District's COVID-19 incidence to characterize the current trajectory

Method: Find recent peak and use hockey stick fit to find inflection point afterwards, then use this period's slope to define the trajectory

Hockey stick fit



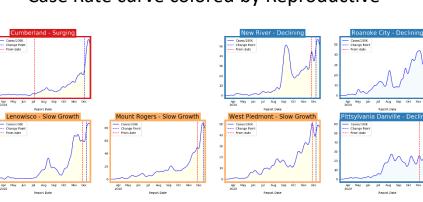
Trajectory	Description	Weekly Case Rate (per 100K) bounds	# Districts (prev week)
Declining	Sustained decreases following a recent peak	below -0.9	12 (2)
Plateau	Steady level with minimal trend up or down	above -0.9 and below 0.5	3 (1)
Slow Growth	Sustained growth not rapid enough to be considered a Surge	above 0.5 and below 2.5	11 (7)
In Surge	Currently experiencing sustained rapid and significant growth	2.5 or greater	9 (25)

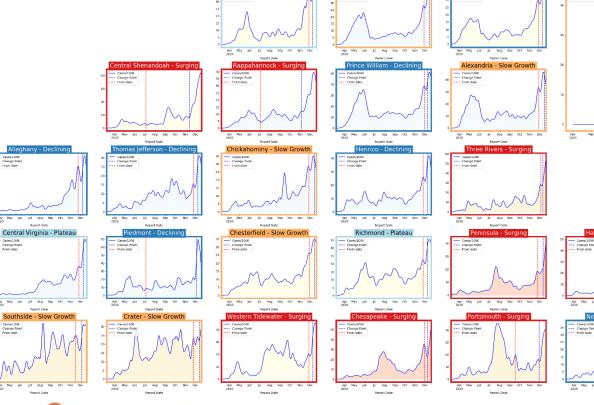


District Trajectories

Status	# Districts (prev week)
Declining	12 (2)
Plateau	3 (1)
Slow Growth	11 (7)
In Surge	9 (25)

Curve shows smoothed case rate (per 100K) Trajectories of states in label & chart box Case Rate curve colored by Reproductive





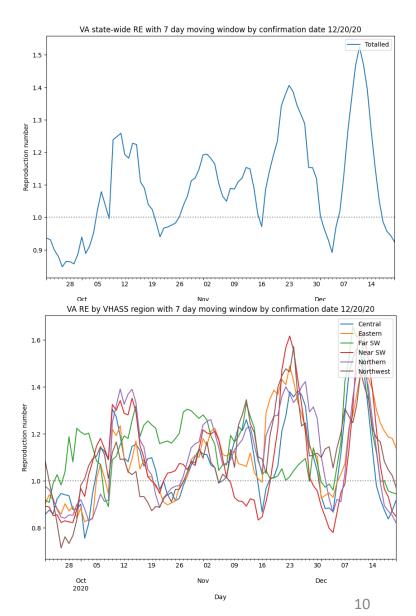
Estimating Daily Reproductive Number

Dec 20th Estimates

Region	Date Confirmed R _e	Date Confirmed Diff Last Week
State-wide	0.924	-0.470
Central	0.918	-0.214
Eastern	1.139	-0.248
Far SW	0.945	-0.258
Near SW	0.848	-0.537
Northern	0.821	-0.436
Northwest	0.972	-0.250

Methodology

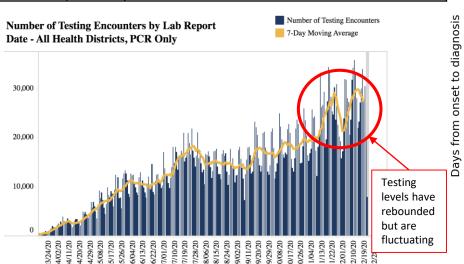
- Wallinga-Teunis method (EpiEstim¹) for cases by confirmation date
- Serial interval: 6 days (2 day std dev)
- Using Confirmation date since due to increasingly unstable estimates from onset date due to backfill



^{1.} Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133

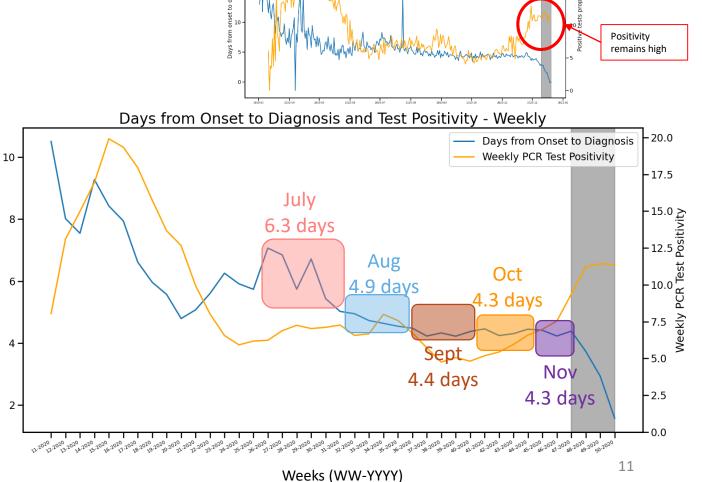
Changes in Case Detection

Timeframe (weeks)	Mean days	% difference from overall mean
April (13-16)	8.3	51%
May (17-21)	5.6	2%
June (22-25)	5.9	7%
July (26-30)	6.4	16%
Aug (31-34)	4.8	-12%
Sept (35-38)	4.4	-20%
Oct (39-43)	4.3	-21%
Nov (44-47)	4.4	-21%
Overall (13-47)	5.5	0%



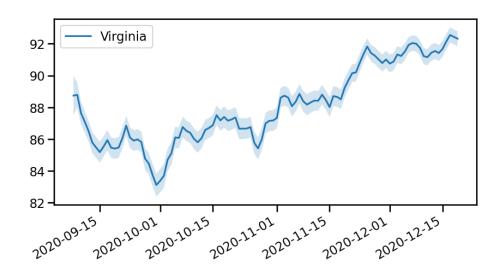
Test positivity vs. Onset to Diagnosis Days from Onset to Diagnosis - Daily

 Days from Onset to Diagnosis Test Positivity



22-Dec-20

Mask usage in Virginia



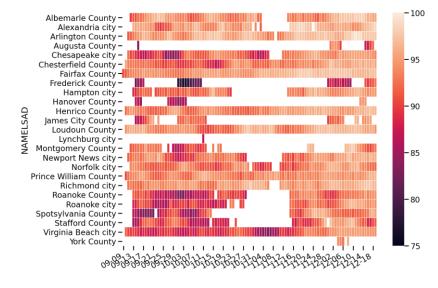
State level mask usage as reported via Facebook surveys over the past month shows ranges from 83% to 91%

Relatively stable over time

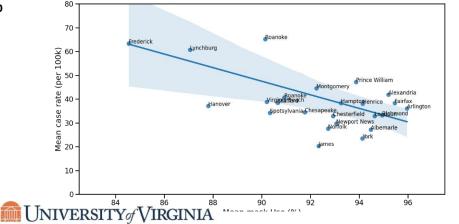
Limited variance across the commonwealth

~3000 daily responses from VA

Data Source: https://covidcast.cmu.edu



Some county level fluctuations since beginning of Sept., though data quality may be affected by sample sizes.



Correlations seen among VA counties between mask use and case rate are now stronger due to surging growth

Slope: - 2.85; for every % we see a ~3/100K case rate difference

Health Care Worker Prevalence (per 100K)

Point Prevalence HCW Point Prevalence by Zip Code High: 3000+ (2020-12-19)**Case Rates among health workers** 2000 Frederick Loudoun 1000 Based on census counts of patient-facing health care workers (Practitioners Low: 0 Units = Active Cases / 100,000 Fairfax and Technologists) Rockingham Prevalence rate for week ending Dec 19 Culpeper Stafford Highland Orange Many areas have high burden on HCW, Augusta especially southern VA Bath Caroline Louisa Albemarle Rockbridge Nelson Hanover Accomack Buckingham Botetourt Powhatan Amelia Bedford Buchanan Campbell Mont. Bland Nottoway Tazewell Dinwiddie Pulaski Charlotte Franklin Lunenburg Russell Floyd Wythe Sussex Smyth Halifax Brunswick Carroll Washington Scott Mecklenburg Patrick Grayson Henry

Ascertainment Rate = 1



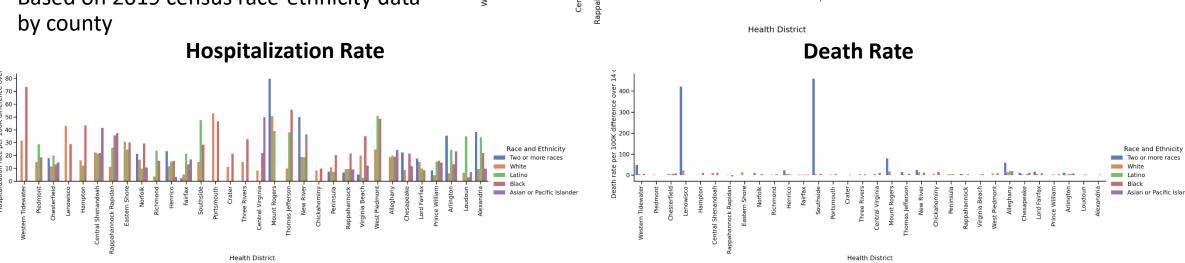
Race and Ethnicity — Recent Rate Changes (per 100K)

8 1200 -

Case Rate

Recent Changes in Race and Ethnicity Rates (per 100k)

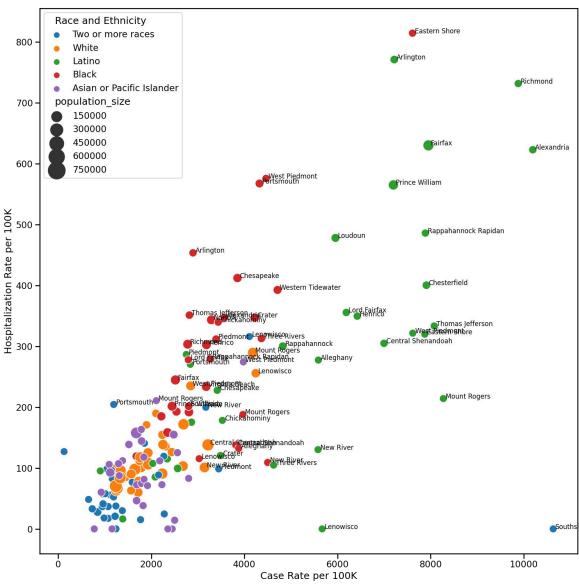
- Two week change in population level rates
- Black, Latinx and 2 or more races populations have much higher changes in rates; disparity is more pronounced in some districts than others
- Based on 2019 census race-ethnicity data by county





Asian or Pacific Islande

Race and Ethnicity cases per 100K



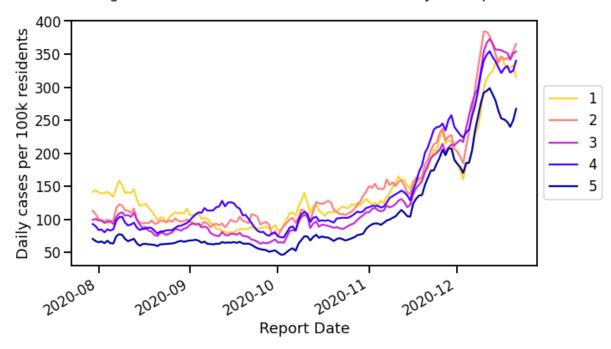
Rates per 100K of each Racial-Ethnic population by Health District

- Each Health District's Racial-Ethnic population is plotted by their Hospitalization and Case Rate
- Points are sized based on their overall population size
- Overlapping labels removed for clarity

22-Dec-20

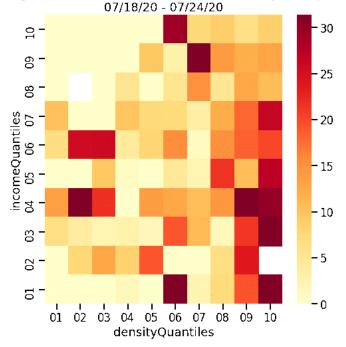
Impact across Density and Income

VDH 7-day moving average rate of new COVID-19 cases by zip code average household income (dollars/ household years) quantile



All zip codes show similar slowing of growth, wealthiest zip codes drop the fastest.

VDH mean cases per 100k by zip code population density (person/ sq mile) and average household income (dollars/ household years) quantiles

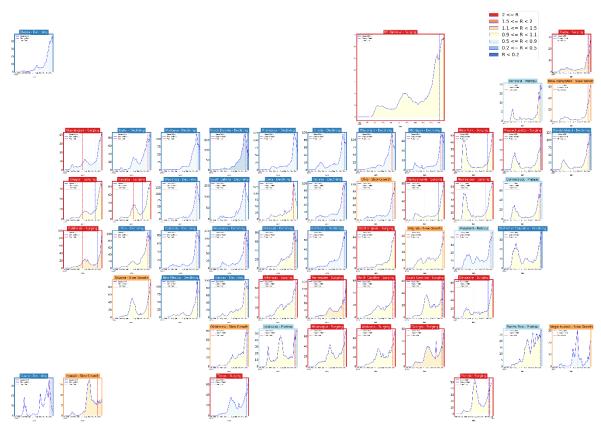


Full evolution of pandemic, shows shifts from denser and wealthier zip codes to poorer and less dense zip codes, followed by a repeat of the pattern. Recently see an uptick across the spectrum of density and income.



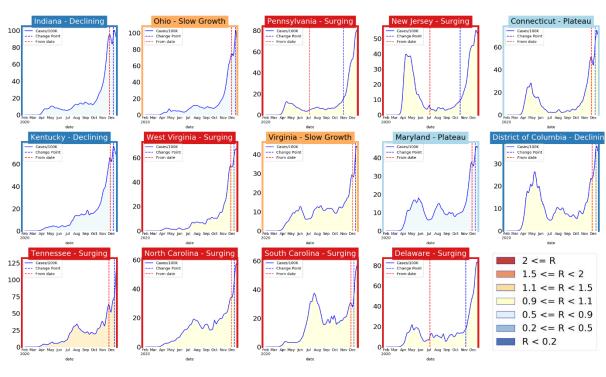
Other State Comparisons

Trajectories of States



Many of the states with huge surges in past 6 weeks (Plains & Midwest) are subsiding

Virginia and her neighbors



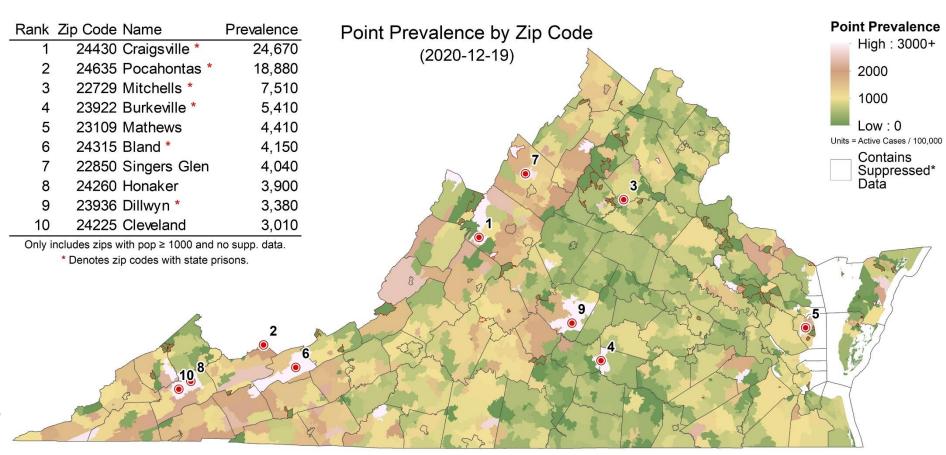
- VA slows its growth
- Many mid-Atlantic states remain in surge (20 total in US)
- Several neighbors have plateaued, though rates remain high
- All states have highest rates of the pandemic in past 2 weeks



Zip code level weekly Case Rate (per 100K)

Case Rates in the last week by zip code

- Concentrations of very high prevalence in many zip codes
- Several of the top ten zip codes are home to prisons
- Southwest has considerable concentration of high prevalence zips
- Some counts are low and suppressed to protect anonymity, those are shown in white

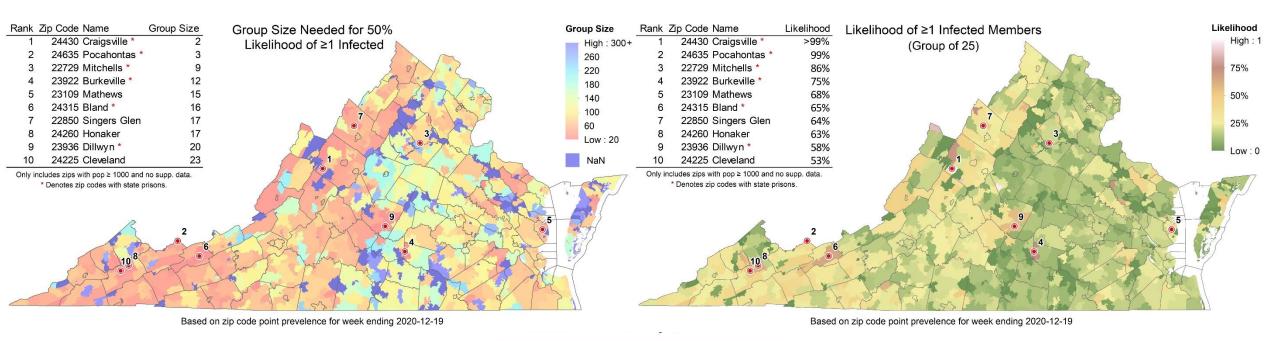




Risk of Exposure by Group Size

Case Prevalence in the last week by zip code used to calculate risk of encountering someone infected in a gathering of randomly selected people (group size 25)

- Assumes 3 undetected infections per confirmed case (ascertainment rate from recent seroprevalence survey)
- On left, minimum size of a group with a 50% chance an individual is infected by zip code (eg in a group of 20 in Staunton, there is a 50% chance someone will be infected)
- Some zip codes have high likelihood of exposure even in groups of 25



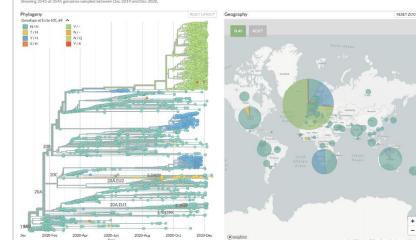
New variant of SARS-CoV2 circulating in UK

Prevalence in the UK of variant with potentially increased transmissibility

but no evidence of higher severity

Aliases: <u>Variant VUI 202012/01</u> and <u>Lineage B.1.1.7</u>

- No direct evidence of this variant in US yet, but recent genomic surveillance in US is limited, it is likely circulating
- This variant is still detected by PCR and is unlikely to alter efficacy of vaccines or other immune treatments
- Evolution expected when virus under selective pressure
- NERVTAG suggests that "<u>VUI-202012/01 demonstrates a substantial increase in transmissibility compared to other variants</u>"
- Mutations include but not limited to
 - (69 Y/-) <u>Two deletions in the spike protein associated with immune evasion</u>; (N501Y) <u>Mutation in the receptor binding domain</u> <u>w/ higher binding affinity w/ ACE2</u>; (P681H) <u>Mutation in the S1/S2 furin cleavage site which promotes entry</u>



nextstrain.org

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Model Update – Adaptive Fitting



Adaptive Fitting Approach

Each county fit precisely, with recent trends used for future projection

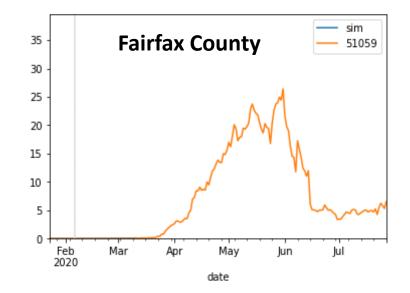
 Allows history to be precisely captured, and used to guide bounds on projections

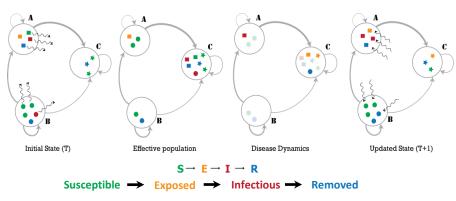
Model: An alternative use of the same meta-population model, PatchSim

- Allows for future "what-if" Scenarios to be layered on top of calibrated model
- Eliminates connectivity between patches, to allow calibration to capture the increasingly unsynchronized epidemic

External Seeding: Steady low-level importation

- Widespread pandemic eliminates sensitivity to initial conditions
- Uses steady 1 case per 10M population per day external seeding



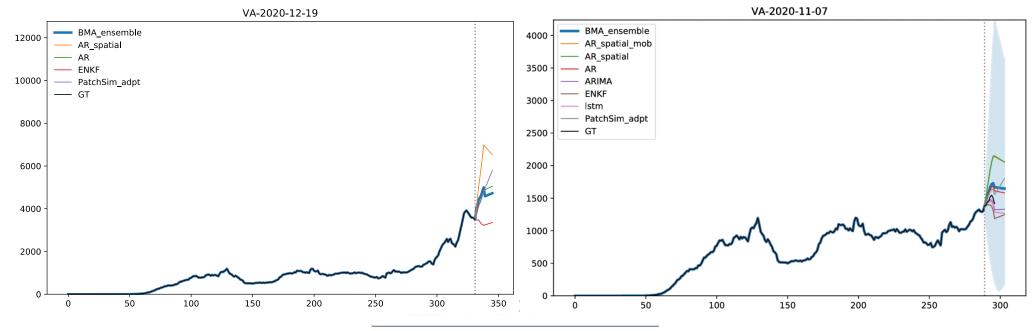




Using Ensemble Model to Guide Projections

An ensemble methodology that combines the Adaptive Fitting and machine learning and statistical models has been developed and refined

- Models: Adaptive Fitting, ARIMA, LSTM, AR, spatially driven AR, Kalman Filters (ENKF)
- This approach facilitates the use of other data streams (weather, mobility, etc.)
- Ensemble provides scaffolding for the Adaptive Fitting's short-term projections



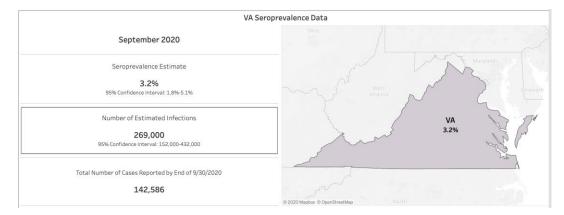
Seroprevalence updates to model design

Several seroprevalence studies provide better picture of how many actual infections have occurred

- Virginia Serology Study estimated 2.4% of Virginians estimated infected (as of Aug 15th)
- CDC Nationwide Commercial Laboratory Seroprevalence Survey estimated 4.1% [2.4% – 6.2%] seroprevalence as of Oct 9th-21st up from 3.2% a month earlier

These findings are equivalent to an ascertainment ratio of ~3x, with bounds of (1x to 7x)

- Thus for 3x there are 3 total infections in the population for every confirmed case
- Uncertainty design has been shifted to these bounds (previously higher ascertainments as was consistent earlier in the pandemic were being used)



https://covid.cdc.gov/covid-data-tracker/#national-lab

Virginia Coronavirus Serology Project Interim findings by region and statewide - July 22, 2020

		Nombon	Crude Weighted pre		lence*
Region	Number of participants	Number antibody positive	prevalence per 100 participants	per 100 population	(95% CI)
Central	400	8	2.0	3.0	(0.5, 5.5)
East	707	9	1.3	1.5	(-0.2, 3.2)
Northern	819	36	4.4	4.2	(2.5, 5.9)
Northwest	756	11	1.5	0.9	(0.2, 1.6)
Southwest	431	3	0.7	1.0	(-0.2, 2.1)
Virginia	3,113	67	2.2	2.4	(1.6, 3.1)

^{*} Weighted prevalence is reweighted by region, age, sex, race, ethnicity, and insurance status to match census population.

https://www.vdh.virginia.gov/content/uploads/sites/8/2020/08/VDH-Serology-Projects-Update-8-13-2020.pdf



Calibration Approach

- Data:
 - County level case counts by date of onset (from VDH)
 - Confirmed cases for model fitting
- Calibration: fit model to observed data and ensemble's forecast
 - Tune transmissibility across ranges of:
 - Duration of incubation (5-9 days), infectiousness (3-7 days)
 - Undocumented case rate (1x to 7x) guided by seroprevalence studies
 - Detection delay: exposure to confirmation (4-12 days)
 - Approach captures uncertainty, but allows model to precisely track the full trajectory of the outbreak
- **Project:** future cases and outcomes generated using the collection of fit models run into the future
 - Mean trend from last 14 days of observed cases and first week of ensemble's forecast used
 - Outliers removed based on variances in the previous 3 weeks
 - 2 week interpolation to smooth transitions in rapidly changing trajectories

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COVID-19 in Virginia:

Dashboard Updated: 12/22/2020 Data entered by 5:00 PM the prior day.

		Cases, Hospitaliza	ations and Deaths		
Total (Tot Hospitali		Tot Dea	
(New Cases: 3,591)^		17,083		4,705	
Confirmed† 268,472	Probable† 46,009	Confirmed† 16,563	Probable† 520	Confirmed† 4,221	Probable†

^{*} Includes both people with a positive test (Confirmed), and symptomatic with a known exposure to COVID-19 (Probable).

Source: Cases - Virginia Electronic Disease Surveillance System (VEDSS), data entered by 5:00 PM the prior day

Outbreaks		
Total Outbreaks*	Outbreak Associated Cases	
1,836	41,727	

Testing (PCR Only)			
Testing Encounters PCR Only*	Current 7-Day Positivity Rate PCR Only**		
3,993,232	11.4%		

^{*} PCR" refers to "Reverse transcriptase polymerase chain reaction laboratory testing.

^{**} Lab reports may not have been received yet. Percent positivity is not calculated for days with incomplete data.

Multisystem Syndrome	Inflammatory in Children
Total Cases*	Total Deaths
12	0

^{*}Cases defined by CDC HAN case definition: https://emergency.cdc.gov/han/2020/han00432.asp

Accessed 10:00am December 22, 2020

https://www.vdh.virginia.gov/coronavirus/

^{**} Hospitalization status at time case was investigated by VDH. This underrepresents the total number of hospitalizations in Virginia

New cases represent the number of confirmed and probable cases reported to VDH in the past 24 hours.

[†] VDH adopted the updated CDC COVID-19 confirmed and probable surveillance case definitions on August 27, 2020. Found here: https://wwwn.cdc.gov/nndss/conditions/coronavirus-disease-2019-covid-19/case-definition/2020/08/0

Scenarios – Seasonal Effects and Vaccines

- Societal changes in the past month have led to an increase in transmission rates, these could continue to drive transmission
 - Seasonal impact of weather patterns, viral mutations, interactions at places of learning, travel related to holidays and traditional large family gatherings, fatigue with infection control practices
 - Population's behaviors determine the level of control of transmission we can achieve
- Vaccination has started, focus on priority groups may limit population level effects initially, though small impacts may be observed in early February
 - Initial rollout estimated at 12.5M people in US (~330K in VA) in January, then 25M (~660K) per month, assumes limited impact from any vaccinations in December.
 - Assume all available vaccine is administered and has 80% efficacy in 2 weeks (timing more sensitive than max efficacy in early stages)
 - Counterfactuals with no vaccine ("NoVax") are provided for comparison purposes



Scenarios – Seasonal Effects and Vaccines

- Three behavioral scenarios capture possible trajectories starting Dec 24th, 2020
 - Adaptive: No change from base projection
 - Adaptive-MoreControl: 15% decrease in transmission starting Dec 24th, 2020
 - Adaptive-LessControl: 15% increase in transmission starting Dec 24th, 2020
- Vaccinations are incorporated in "base" projections, counterfactuals without vaccinations provide lower bound on vaccines impact
 - Adaptive-NoVax: No change from base projection without vaccine
 - Adaptive-NoVax-MoreControl: 15% decrease in transmission starting Dec 24th, 2020 without vaccine
 - Adaptive-NoVax-LessControl: 15% increase in transmission starting Dec 24th, 2020 without vaccine

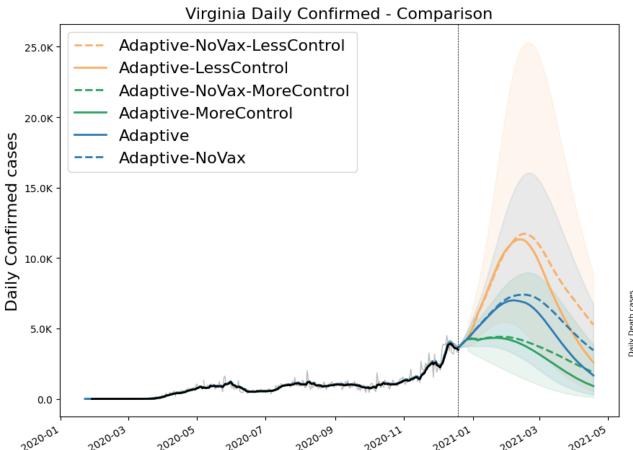


Model Results

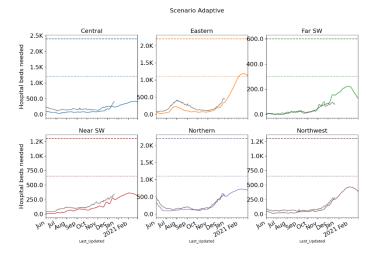


Outcome Projections

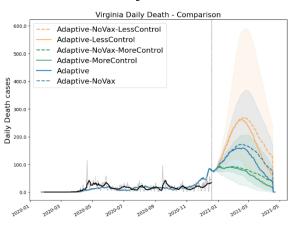
Confirmed cases



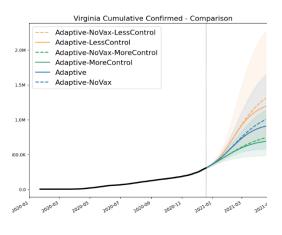
Estimated Hospital Occupancy



Daily Deaths



Cumulative Confirmed cases



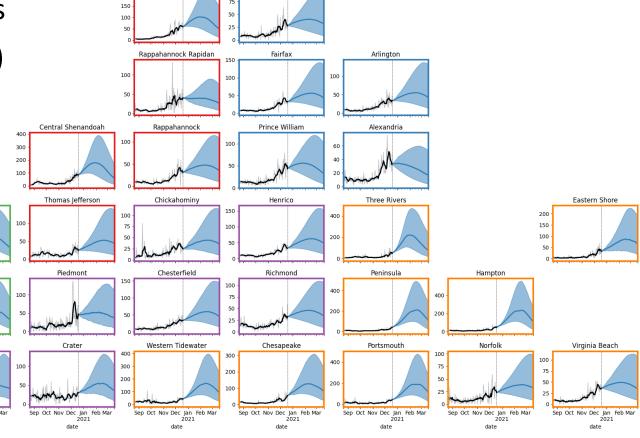


District Level Projections: Adaptive

Adaptive projections by District

Projections that best fit recent trends

 Daily confirmed cases rate (per 100K) by Region (blue solid) with simulation colored by scenario





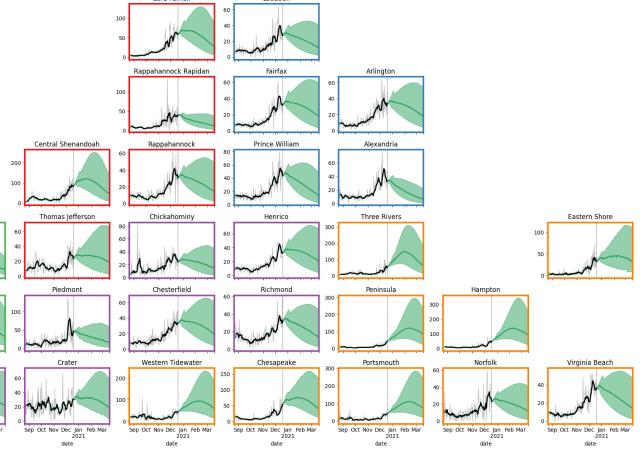
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District Level Projections: Adaptive-MoreControl

Adaptive projections by District

Projections that best fit recent trends

 Daily confirmed cases rate (per 100K) by Region (blue solid) with simulation colored by scenario





Cumberland

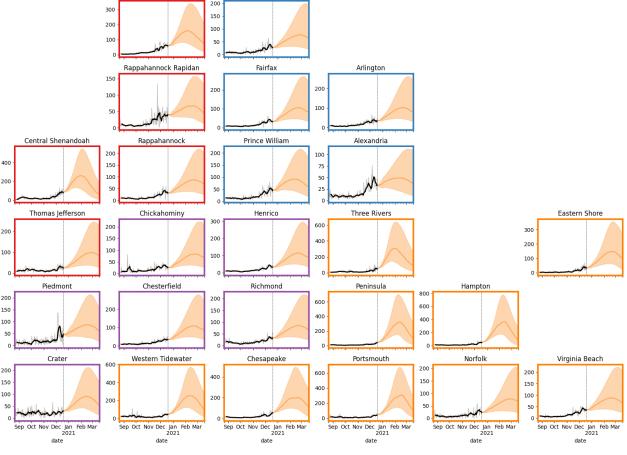
District Level Projections: Adaptive-LessControl

Adaptive projections by District

Projections that best fit recent trends

 Daily confirmed cases rate (per 100K) by Region (blue solid) with simulation colored by scenario

150





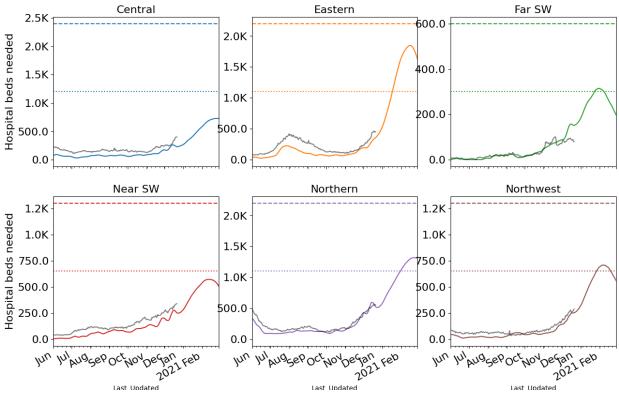
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Cumberland

Hospital Demand and Bed Capacity by Region

Capacities* by Region – Adaptive-LessControl

COVID-19 capacity ranges from 80% (dots) to 120% (dash) of total beds



Week Ending	Adaptive	Adaptive- LessControl
12/20/20	25,271	25,275
12/27/20	27,183	27,248
1/3/20	31,078	33,457
1/10/20	35,210	42,901
1/17/20	39,232	52,077
1/24/20	42,980	61,541
1/31/20	45,777	69,334
2/7/20	47,125	74,202
2/14/20	46,901	76,371
2/21/20	45,690	74,913
2/28/20	42,910	69,637
3/7/20	38,745	61,531

Weekly confirmed cases

If Adaptive-LessControl scenario persists:

- All regions approach initial bed capacity this winter
- Surge capacity exceeded in Northern region, in mid-Jan to early March



^{*} Assumes average length of stay of 8 days 22-Dec-20

Key Takeaways

Projecting future cases precisely is impossible and unnecessary. Even without perfect projections, we can confidently draw conclusions:

- Case rate growth in Virginia slows and steadies with mixed patterns across commonwealth
- VA mean weekly incidence (43/100K) steady (from 44) as national surge slows and is slightly down for first week in months (to 59/100K from 66/100K).
- Recent updates:
 - Preliminary estimates for vaccination impact
 - Planning scenarios remain on Christmas holiday, Dec 24th
- Behavioral changes can outpace impact of optimistic vaccine rollout and prevent significantly more cases by Spring
- The situation is changing rapidly. Models will be updated regularly



References

Venkatramanan, S., et al. "Optimizing spatial allocation of seasonal influenza vaccine under temporal constraints." *PLoS computational biology* 15.9 (2019): e1007111.

Arindam Fadikar, Dave Higdon, Jiangzhuo Chen, Bryan Lewis, Srinivasan Venkatramanan, and Madhav Marathe. Calibrating a stochastic, agent-based model using quantile-based emulation. SIAM/ASA Journal on Uncertainty Quantification, 6(4):1685–1706, 2018.

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Biocomplexity Institute. COVID-19 Surveillance Dashboard. https://nssac.bii.virginia.edu/covid-19/dashboard/

Google. COVID-19 community mobility reports. https://www.google.com/covid19/mobility/

Biocomplexity page for data and other resources related to COVID-19: https://covid19.biocomplexity.virginia.edu/



Questions?

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Biocomplexity COVID-19 Response Team

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Supplemental Slides



Estimating Daily Reproductive Number

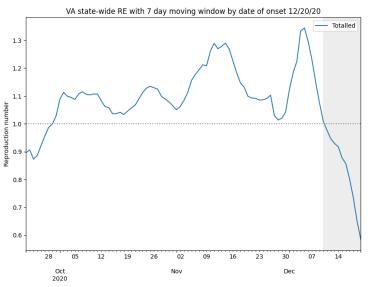
Dec 11th Estimates

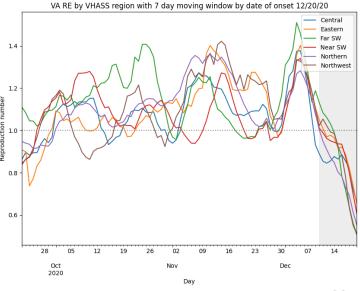
Region	Date of Onset R _e	Date Onset Diff Last Week
State-wide	0.977	-0.275
Central	0.854	-0.491
Eastern	1.009	-0.176
Far SW	1.083	-0.323
Near SW	0.988	-0.301
Northern	0.949	-0.253
Northwest	1.054	-0.193

Methodology

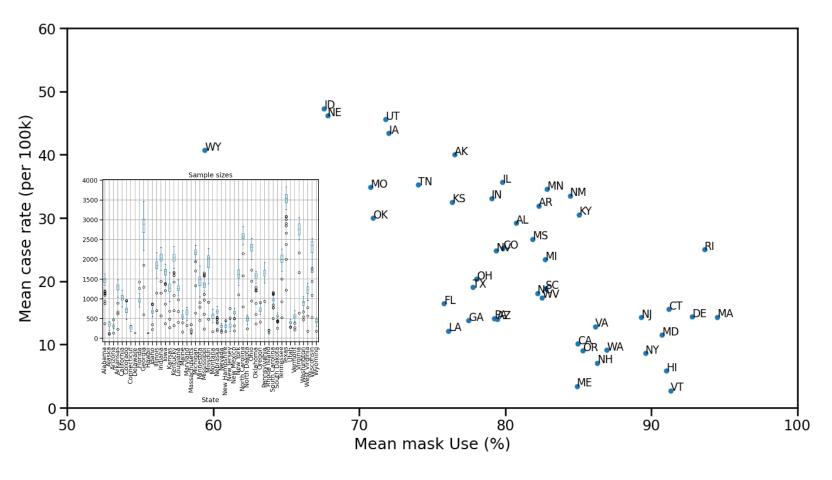
- Wallinga-Teunis method (EpiEstim¹) for cases by date of onset
- Serial interval: 6 days (2 day std dev)
- Recent estimates may be unstable due to backfill

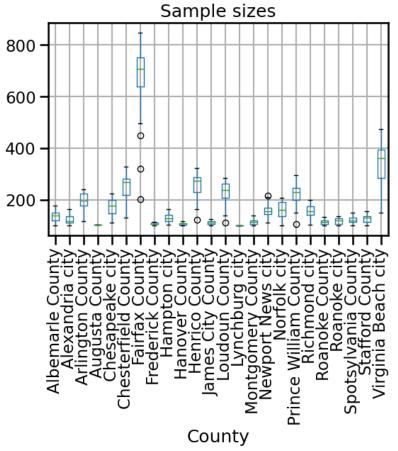
1. Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133





Mask usage sample sizes



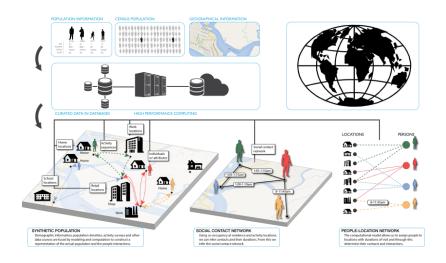


22-Dec-20

Agent-based Model (ABM)

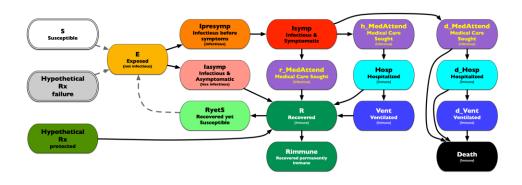
EpiHiper: Distributed network-based stochastic disease transmission simulations

- Assess the impact on transmission under different conditions
- Assess the impacts of contact tracing



Synthetic Population

- Census derived age and household structure
- Time-Use survey driven activities at appropriate locations



Detailed Disease Course of COVID-19

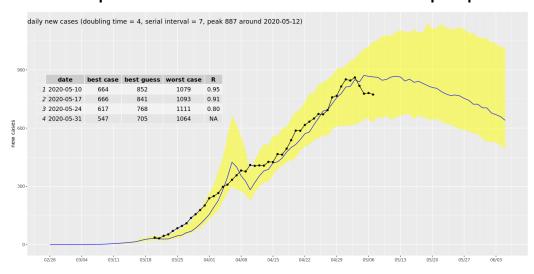
- Literature based probabilities of outcomes with appropriate delays
- Varying levels of infectiousness
- Hypothetical treatments for future developments



ABM Social Distancing Rebound Study Design

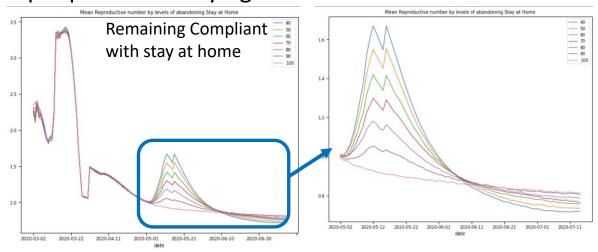
Study of "Stay Home" policy adherence

- Calibration to current state in epidemic
- Implement "release" of different proportions of people from "staying at home"



Calibration to Current State

- Adjust transmission and adherence to current policies to current observations
- For Virginia, with same seeding approach as PatchSim



Impacts on Reproductive number with release

- After release, spike in transmission driven by additional interactions at work, retail, and other
- At 25% release (70-80% remain compliant)
- Translates to 15% increase in transmission, which represents a 1/6th return to pre-pandemic levels



Medical Resource Demand Dashboard

https://nssac.bii.virginia.edu/covid-19/vmrddash/

